REMARKS

Claims 1, 2, 4, 5, 7, 9, 11-13 and 20-28 are presently pending. Of these, Claims 13 and 20-28 are withdrawn from consideration. Amendments to the claims are discussed below. No new matter has been added herewith. The following addresses the substance of the Office Action.

Written Description

Claims 1, 2, 4, 5, 7, 8, 9, 11 and 12 were rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. The Examiner correctly interpreted that only one D may be attached to E at one site, and that the linker can contain additional sugar moieties apart from D. However, the amended claims were found to be broader than the previous claim and the description in the specification because the additional sugar moieties were not limited or defined. The Examiner noted that the specification requires that D is selected from D-manose, D-galactose, D-glucose, Dglucosamine, N-acetylglucosamine and 6-deoxy-L-mannose, but the additional sugars recited in the claims were not limited to these. The Examiner stated that the specification supports inclusion of additional sugar moieties which fall within the definition of D, but not additional sugar moieties which fall outside of that definition.

The Applicant has further defined spacer or linker group E. In addition to group D, the linker may also attach to a second sugar moiety designated G. The specification states at page 8 that D comprises at least one sugar moiety selected from the group comprising D-mannose, D-galactose, D-glucose, Dglucosamine, N-acetylglucosamine and 6-deoxy-L-mannose, wherein when D is more than one sugar moiety, the sugar moiety may comprise a single chain of the same or different sugar moieties, or may comprise two or more separate sugar moieties or chains of sugar moieties attached to D at different sites. In the amended claims both D and G are defined as independently consisting of a glycosyloxy or oligoglycosyloxy sugar moiety wherein the sugar is selected from the group consisting of D-mannose, D-galactose, D-glucose, D-glucosamine, Nacetylglucosamine, and 6-deoxy-L-mannose, wherein an oligoglycosyloxy sugar moiety may comprise the same or different sugars. Therefore, the specification provides written support for the additional sugar moieties provided in group G. Amended Claim 1 is no broader in scope than the original claim. In fact, amended Claim 1 is actually more limited, as the sugar groups can now only be attached to the spacer group E at defined positions. The amended claim does not encompass any compounds that were not claimed by the former claim. In addition, the options

for E of "$-C_aHR_3$-C_bHR_4-" and "cyclohexyl optionally substituted with one or more G groups" have been deleted from the claims.

The Examiner also commented that Claim 8 had been amended to comprise an "α-1,2 and/or α-1,6 linked sugar moiety". Since the claim also includes "an oligosaccharide chain of 2 to 12 α-1,2 and/or α-1,6 linked sugar moieties, the Examiner considered that the amendment broadened the definition of D beyond 2 to 12 linked sugar moieties. In the interests of expediting prosecution, the Applicant has limited the oligosaccharide chains of D and G in Claim 1 to chains of 2 to 12 sugar units and Claim 8 is canceled. For consistency with Claim 1, Claim 9 is amended to specify "α-1,2 and/or α-1,6 linked sugars".

In view of the amendments to the claims and the foregoing remarks, the claims are believed to be in compliance with the written description requirement of 35 U.S.C. § 112, first paragraph. Accordingly, the Applicant respectfully requests that the rejection be withdrawn.

Anticipation

Kenkyusho

Claims 1, 2, 4, 5, 7, 9 and 12 were rejected under 35 U.S.C. § 102(b) as being anticipated by Kenkyusho (JP 06271597). The claims have been amended to exclude compounds with a simple ethylene spacer group by removal of the option "$-C_aHR_3$-C_bHR_4-" from group E. Kenkyusho does not describe any of the claimed compounds, which now all contain at least two carbohydrate moieties attached to the spacer group.

To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed.Cir. 1986). "[A]nticipation requires that all of the elements and limitations of the claim are found within a single prior art reference." *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991). Since the reference does not teach each and every element of the presently claimed molecules, the reference does not anticipate the claims.

Sanderson et al.

Claims 1, 5, 7, 9 and 12 were rejected under 35 U.S.C. § 102(b) as being anticipated by Sanderson et al. (1982 *J Biol Chem* **237**:3603-3613). The Examiner interpreted the compound of Figure 14 as fitting within the scope of the claims when:

-A is R where R is H,

-E is -C_aHR_3-C_bHR_4 wherein R_3 is H, R_4 is -$(CH(OH))_m$-CH_20H, m is 2 and

-D is N -acetylglucosamine.

The claims have been amended to remove "–C_aHR_3-C_bHR_4-" as an option for E. In addition, Claim 1 is amended to remove H as an option for R where A is R. Sanderson et al. does not disclose any compounds where R is a glyceride group of formula Ia or Ib or where R is a linear or branch alkyl of up to 40 carbon atoms, nor compounds where two or more carbohydrate groups are attached via a linker to a phosphate group. Accordingly, the presently claimed molecules are not anticipated by the reference.

Obviousness

Claim 8 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Kenkyusho (*supra*). The Examiner stated that it would have been obvious to prepare compounds having 2-12 linked sugar moieties because Kenkyusho teaches that oligosaccharide derivatives are also suitable.

Claim 8 is canceled and the limitation of former Claim 8 is incorporated into Claim 1. As discussed above, Kenkyusho does not disclose compounds within the scope of Claim 1 (i.e., which all contain at least two carbohydrate moieties attached to the spacer group E). Based on Kenkyusho, the skilled artisan would have had no reason to arrived at the presently claimed compounds, which all have at least two carbohydrate moieties attached to the spacer group E. Accordingly, the presently claimed compounds are not *prima facie* obvious in view of Kenkyusho.

Additional Distinctions between the Presently Claimed Compounds and the Compounds of Kenkyusho

Kenkyusho describes compounds comprising mono- or oligo-saccharides bound to a phosphoric acid lipid ester for use in modifying liposome drug carriers. The liposomes use a lipid derivative of sugar as a homing device to target the liposome to an organ. The compounds of the Kenkyusho document, compounds 4-9 and 4-19 in particular, comprise four structural elements:

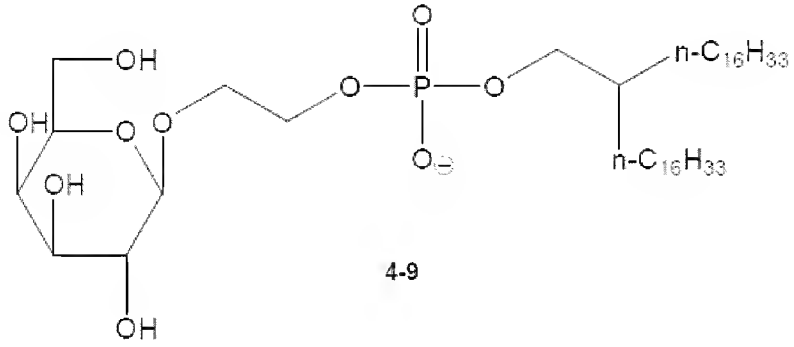
a) a sugar moiety (specifically a beta-galactopyranosyloxy group in both compounds 4-9 and 4-19),

b) a two-carbon atom linker moiety (specifically a 1,2-ethylene linker in both compounds 4-9 and 4-19),

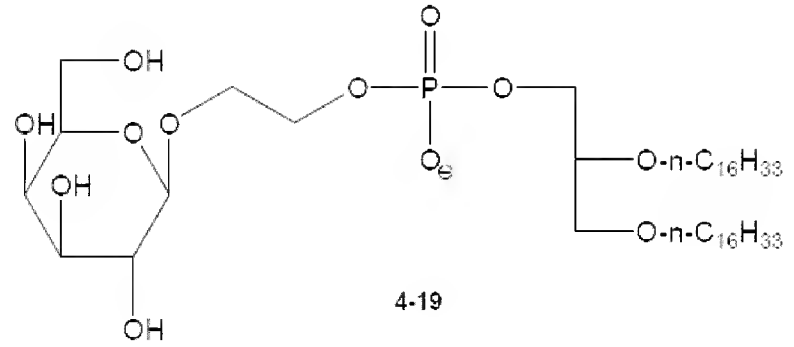
c) a diesterified phosphate (in both compounds 4-9 and 4-19), and

d) a lipid moiety (a branched alkyl in the case of compound 4-9, a dialkylglyceryl in the case of compound 4-19)

Each of these structural elements is arranged in a linear sequence.



4-9



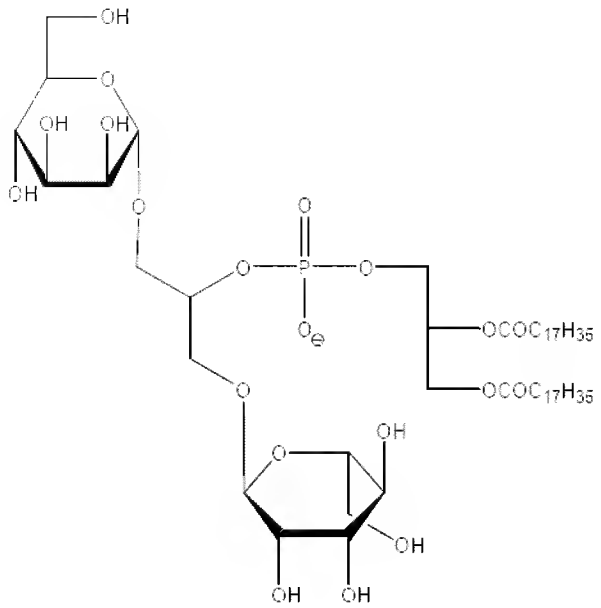
4-19

The compounds of Formula I of Amended Claim 1 differ chemically from the compounds of the Kenkyusho document with regard to two of these aspects:

1) there are at least two separate sugar moieties, and

2) the linker moiety has at least three carbon atoms.

Further, the structural elements are not connected in a linear sequence but rather in a branched manner. Such compounds are exemplified by compound 15 of the present application:



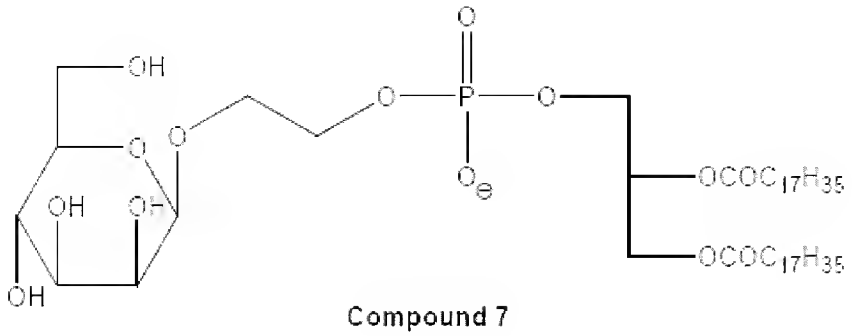
Compound 15

Thus the compounds of Claim 1 are significantly different in at least three distinct aspects from those of Kenkyusho. These structural differences confer properties on the compounds of formula I that would make them unsuitable for imparting liposomes with directivity to an organ. Biomolecular recognition of the liposome drug carrier is achieved by the sugar functionality on the glycophospholipids of the liposome. The sugar functionality can act as a ligand for various receptors on the target organ.

The characteristics of the ligand-receptor interactions are at least partially based on the structural features of the phospholipids of the liposome. These structural features dictate, at least in part, the interaction of the liposome with its surrounding microenvironment. Factors such as the polarity of the head group, the proximity of the phospholipid portion to the sugar reside, the rotational flexibility of the component groups, and the number of sugar residues can be expected to have a major influence on the way that a glycophospholipid influences the properties of a liposome in which it forms a part.

For example, a person skilled in the art would expect that addition of a second sugar residue to a glycophospholipid such as 4-19 would change the polarity and other properties to

such an extent that it would no longer be predictable that the compound would successfully incorporate into a liposome so as to induce the liposome to target an organ. For Example, Compound 7 of the present application contains the same four structural elements of the Kenkyusho compounds and which are also arranged linearly:



Compound 7

This compound was found to have poor aqueous solubility. As shown in the footnote to Table 4 in the present specification (see page 68), Compound 7 required the use of the non-ionic detergent, Tween, in order to be dissolved for the *in vitro* assay. Given the close structural similarity between Compound 7 and 4-19 from Kenkyusho, it would be expected that 4-19 would also have poor aqueous solubility. This property would be expected and necessary in a glycophospholipid to be incorporated into a membrane structure stable enough to induce the resulting liposome to target an organ.

However, the introduction of branching, combined with the presence of at least two separate sugar moieties attached to a three carbon atom linker would be expected to greatly increase the water solubility of the compound, making it unsuitable for this application. Therefore, a person skilled in the art seeking alternative glycolphospholipids for liposome modification would not be motivated to modify the Kenkyusho compounds so as to make a compound of the present invention. In addition, Kenkyusho provides no motivation to add additional sugar moieties in a branching manner, to the compounds described therein. To do so would add additional chemical complexity necessitating additional synthetic steps, without affording any advantageous features.

In view of the preceding remarks, the Applicant respectfully requests that the rejection under 35 U.S.C. § 103(a) be withdrawn.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

In view of Applicants' amendments to the Claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: August 2, 2010

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